REMARKS

Applicant has already received a Notice of Allowance in respect of the present application. After receiving the Notice of Allowance, Applicant became aware that there are minor clerical errors in the specification and claims of the present application. In particular, in the R_1 substituent in the chemical structure of Formula I in Claim 1, the number "1" is subscript when it should be superscript. The same applies to page 3 of the specification. Applicant has amended Claim 1 and page 3 of the specification of the present application by changing the script of the number "1" in the R_1 substituent in the chemical structure of Formula I from subscript to superscript. New replacement page 3 of the specification is submitted herewith. Support for this amendment can be found in the specification and claims as originally filed. No new subject matter has been added.

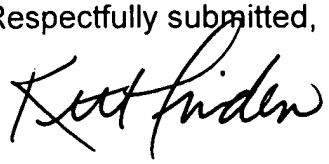
As well, there is an improper paragraph return at the end of line 28 on page 38 of the specification. Applicant has amended page 38 of the specification and new replacement page 38 of the specification is submitted herewith. No new subject matter has been added.

Further, Applicant has deleted the statement, "Symmetry transformations used to generate equivalent atoms: #1 -x, -y+1,-z" from lines 40 to 41 on page 58 of the specification and the statement "Symmetry transformations used to generate equivalent atoms:" from line 11 on page 62 of the specification. X-ray crystallography cannot generate information on the hydrogen atom. Thus, the crystallographer has to use computational means to add back the hydrogen atom for the final co-ordinates. These statements report the symmetry transformation model used by the crystallographer to add back the hydrogen atom. However, the data in Tables 6 and 8 of the specification do not provide any data on the hydrogen atoms. This has no impact on the experimental data provided therein. Therefore, the deleted statements are irrelevant to the data provided and this is why they have been deleted. New replacement pages 58 and 62 of the specification are submitted herewith. No new subject matter has been added.

In respect of the above amendments, Applicant is of the opinion that they are minor in nature and do not touch the merits and thus Applicant requests that these amendments

be entered on the recommendation of the Primary Examiner, approved by the Director, without withdrawing the application from issue. Should the Examiner have any questions, she is respectfully requested to contact Applicant's Agent, Kitt Sinden, collect, at 905-771-6414, at her convenience.

Respectfully submitted,



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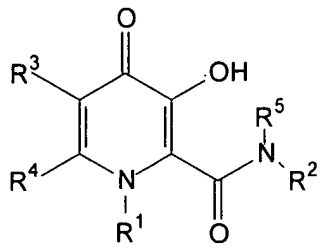
Enclosures: Pages 3, 38, 58 and 62 of the Specification

amide hydrochloride), the dimethylcarbamoyl analogue. CP502, CP506 and CP508 are prior art and have not been evaluated in humans.

SUMMARY OF THE INVENTION

A first aspect of the present invention provides a 3-hydroxypyridin-4-one compound of formula I inclusive of a pharmaceutically acceptable salt of the compound of formula I,



I

wherein:

R^1 is X with the proviso that R^2 is Y;

or

R^1 is T with the proviso that R^2 is W;

or

R^1 is X with the proviso that R^2R^5N when taken together, form a heterocyclic ring selected from piperidinyl, morpholinyl, pyrrolidinyl or piperazinyl, wherein the group piperidinyl, morpholinyl, pyrrolidinyl or piperazinyl is either unsubstituted or substituted with one to three C_1-C_6 alkyl groups;

X is C_3-C_6 cycloalkyl;

Y is selected from the group consisting of C_3-C_6 cycloalkyl, C_1 to C_6 alkyl and C_1 to C_6 alkyl monosubstituted with a C_3-C_6 cycloalkyl;

T is C_1 to C_6 alkyl;

W is C_3-C_6 cycloalkyl;

R^3 is selected from the group consisting of hydrogen and C_1-C_6 alkyl;

R^4 is selected from the group consisting of hydrogen and C_1-C_6 alkyl; and

R^5 is selected from the group consisting of hydrogen and C_1-C_6 alkyl.

A second aspect of the present invention provides use of a compound of formula I in the treatment of iron overload related disease.

Shaking Incubator at 25°C and at 90 RPM overnight. The sample solutions were centrifuged at 4000 rpm for 15 minutes, and then placed back in the incubator at 25°C without shaking. The UV-Vis spectrum was recorded at 25°C for each of the 12 solutions.

A Job's plot was created with the absorbance at 450 nm as the y-axis and α as the x-axis. A maximum absorbance was found at α = 0.75, which corresponds to an iron : ligand ratio of 1:3 in the complexes. The Job's plot result is shown in Fig. (1).

Proceeding in a similar manner, the Job's plots of Fe-Apo6617 and Fe-Apo6619 were created. They are shown in Fig. (2) and (3).

EXAMPLE 13: Distribution coefficient determination

MOPS buffer (50 mM, pH=7.4) and 1-octanol were used as the aqueous phase and the organic phase, respectively, for distribution coefficient determinations. The MOPS buffer and 1-octanol were pre-saturated with each other before use.

In a typical experiment, an organic stock solution of Apo6618 (1-cyclopropyl-3-hydroxy-6-methyl-4-oxo-1,4-dihydro-pyridine-2-carboxylic acid cyclopropylamide) was prepared by weighing out 0.50 mg of the compound into a 10-mL volumetric flask and bringing to volume with 1-octanol. The solution was then sonicated for 60 minutes so that the sample could dissolve completely. The concentration of the stock solution was calculated as C^0_{org} = 2.0 x 10^{-4} M. The organic standard solution of Apo6618 with 2.0 x 10^{-5} M was prepared in a 10-mL volumetric flask by 10 times dilution of the stock solution with 1-octanol. The sample solution was prepared in a 10-mL volumetric flask. The stock sample solution (3 ml) was pipetted into the flask followed by the addition of MOPS buffer (3 ml). The standard and sample solutions were then vortexed for 2 hours. After vortexing, the solutions were transferred to test tubes and centrifuged at 4000 rpm for 15 minutes. UV-Vis spectra were recorded for the standard solution and the organic (top) phase of the sample solution at 22°C. The distribution coefficient, $D_{7.4}$, was calculated using the following equation:

C(20)-N(4)-C(21)	126.2(5)		C(28)-C(27)-C(31)	120.9(3)
C(23)-C(21)-N(4)	120.5(8)		N(5)-C(27)-C(31)	118.6(3)
C(23)-C(21)-C(22)	56.8(7)		O(8)-C(28)-C(27)	123.8(3)
N(4)-C(21)-C(22)	118.0(7)		O(8)-C(28)-C(24)	116.6(3)
C(23)-C(22)-C(21)	59.5(7)		C(27)-C(28)-C(24)	119.5(3)
C(22)-C(23)-C(21)	63.7(8)		O(9)-C(31)-N(6)	123.8(4)
C(22*)-C(21*)-C(23*)	63.7(8)		O(9)-C(31)-C(27)	121.5(3)
C(21*)-C(22*)-C(23*)	60.4(8)		N(6)-C(31)-C(27)	114.7(3)
C(21*)-C(23*)-C(22*)	55.9(8)		C(31)-N(6)-C(32)	119.2(5)
O(7)-C(24)-C(25)	125.8(3)		C(34)-C(32)-C(33)	60.3(8)
O(7)-C(24)-C(28)	116.6(3)		C(34)-C(32)-N(6)	126.8(9)
C(25)-C(24)-C(28)	117.5(3)		C(33)-C(32)-N(6)	118.8(8)
C(26)-C(25)-C(24)	121.9(4)		C(34)-C(33)-C(32)	57.5(7)
N(5)-C(26)-C(25)	120.1(3)		C(32)-C(34)-C(33)	62.2(7)
N(5)-C(26)-C(29)	118.4(3)		C(33*)-C(32*)-C(34*)	58.7(9)
C(25)-C(26)-C(29)	121.5(4)		C(32*)-C(33*)-C(34*)	64.0(9)
C(28)-C(27)-N(5)	120.4(3)		C(33*)-C(34*)-C(32*)	57.3(8)

N(3)-C(29)-C(31)	119.3(3)		O(9)-C(32)-C(27)	120.8(2)
N(3)-C(29)-C(30)	118.4(3)		N(6)-C(32)-C(27)	115.4(3)
C(31)-C(29)-C(30)	60.6(2)		C(2S)-N(1S)-C(1S)	119.6(5)
C(29)-C(30)-C(31)	59.7(2)		C(2S)-N(1S)-C(3S)	117.8(4)
C(29)-C(31)-C(30)	59.7(2)		C(1S)-N(1S)-C(3S)	122.5(5)
O(9)-C(32)-N(6)	123.8(3)		O(1S)-C(2S)-N(1S)	120.9(6)